Nearly half of all deaths from prostate cancer can be predicted before age 50

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Focusing prostate cancer testing on men at highest risk of developing the disease is likely to improve the ratio between benefits and the harms of screening, suggests a paper published today in *BMJ*.

Prostate specific antigen (PSA) screening is widely used for the early detection of prostate cancer, but remains highly controversial, as it became widespread long before evidence to prove its value. There is now evidence that PSA screening can reduce prostate cancer mortality in men who would not otherwise be screened. However, this can come at considerable harm.

As there is little evidence to support many aspects of screening guidelines, researchers from Sweden and the USA carried out a case-control study taking data from the Malmo Preventative Project (MPP) cohort, in an attempt to develop an evidence-based scheme for prostate cancer testing. A previous study from the MPP, published in the *BMJ* in 2010, demonstrated that PSA level at age 60 is strongly predictive of the risk of death from prostate cancer by age 85.

The Malmo cohort included 21,277 men aged 27 to 52 who participated in the MPP between 1974 and 1984. All these men gave a blood sample. A smaller group of these men were then invited to provide a second blood sample about six years later: 4922 (72%) of those re-invited complied.

The researchers focused their studies on men close to age 40, mid-to-late

forties (45-49) and early-to-mid fifties (51-55).

Within 25 to 30 years, 44% of deaths from prostate cancer occurred in those with the top 10% of PSA levels at age 45-49, a PSA of about 1.5 ng / ml or more. The risk of prostate cancer death was more than 10 times greater in this group compared to men with the lowest 25% of PSA levels.

The researchers questioned whether PSA screening should start at age 40, mid-to-late 40s or early 50s: they found that even for men with PSA in the top decile at age 40, the risk of metastatic prostate cancer was very low at 0.6%, after 15 years of follow-up. The researchers say that due to this, it would be difficult to justify initiating PSA testing at age 40 for men with no other significant risk factor.

In contrast, the risk of developing metastatic prostate cancer within 15 years is close to three-fold higher for men in the top level PSA at age 45-49 (1.7%) and close to ten-fold higher at age 51-55 (5.2%). This suggests that initiating PSA screening after age 50 would leave a significant proportion of men at elevated risk of later being diagnosed with an incurable cancer.

The researchers also looked at screening intervals: results showed that the absolute risk of metastatic cancer remains very low within 15 years follow-up for men with PSA in the low deciles and as such, a screening interval less than five years for these men is unnecessary.

The researchers conclude that PSA levels are informative of the current risk of cancer as well as being "predictive of the future risk of prostate cancer" and any cancer-specific death. They say that screening programmes can be designed so as to "reduce the risk of over-diagnosis whilst still enabling early cancer detection for men at highest risk of death from prostate cancer". As it turns out, the best way to determine

risk is a single PSA before the age of 50.

More information: Strategy for detection of prostate cancer based on relation between prostate specific antigen at age 40-55 and long term risk of metastasis: case-control study, *BMJ*, 2013.

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